EXHIBIT 3

To
Memorandum In Support of TriPath Imaging, Inc.'s Motion to Exclude Defenses Based on Cytyc's CDS-1000

Civil Action No. 03-11142 [DPW] - Lead Case

Filed May 5, 2005

CONTAINS CONFIDENTIAL INFORMATION SUBJECT TO PROTECTIVE ORDER

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

CYTYC CORPORATION, Plaintiff, v. TRIPATH IMAGING, INC., Defendant.	Civil Action No. 03-11142-DPW [Consolidated Action – Lead Case]
TRIPATH IMAGING, INC., Plaintiff, v. CYTYC CORPORATION, Defendant.	Civil Action No. 03-12630-DPW

EXPERT REPORT OF DR. KENNETH R. CASTLEMAN REGARDING THE INVALIDITY OF U.S. PATENT NOS.

6,327,377 AND 5,257,182

March 7, 2005

present the suspect cell to the cytologist for inspection. It was not intended to make the scanner itself diagnose cancer, but rather to remove much of the monotonous fatiguing screening so that only about 2-3% of microscope fields would need to be reviewed by eye." [Husain III at 198, underlining added]

71. The article also describes that the use IOD alone is insufficient for distinguishing between benign and malignant cell populations. "The measurement, not just of the size and shape of the cell, but of its integrated optical density and total nuclear mass . . . should not fail to detect the tumour cells." [Husain III at 199]

72. The then-current trials involved a Cytoscan 110, which was developed by the Medical Research Council's Clinical and Population Cyotgenetics Unit in Edinburgh, Scotland. The instrument presented suspect cells to a human reviewer in ranked order: "The results also indicate that though the suspicious signals alerted by the machine are ranked in order of severity for operator review, there is a need to reduce false positive signals that require editing to make the system more economic." [Husain III at 200]

3. Development of CDS-1000 in the United States

73. Cytyc developed a partially automated screening device in the late 1980's and early 1990's. I understand that the "CDS" stands for "Computer Directed Screening". As detailed later in this report, the CDS-1000 is another example of a device that scanned cells, ranked the cell images based on predetermined criteria, and presented the images, in ranked order, to an operator for further review and diagnosis.

cytopathologists can easily be expedited since problem cells can be mapped and relocated for a second look." [Greenberg at 171]

265. Claim 14 depends from claim 11 and further cites that the assigning step "comprises assigning a value on a scale between a first output value associated with a first condition and a second output value associated with a second condition." Claim 15 depends from claim 14 and recites that the "first condition is benign and the second condition is non-benign." Greenberg discloses each of these features. Greenberg discloses that:

> The ASI, which is an objective numerical measure of the atypicality of bronchial epithelial cells in sputum, is scaled from 0.5 (squamous metaplasia) to 4.5 (carcinoma) and correlates with the progressive pattern of bronchial epithelial dysplasias observed in the morphogenesis of pulmonary squamous-cell carcinoma. It is computed mathematically by using the composite nuclear and cytoplasmic feature values that best discriminate in a linear fashion between members of a cell population. The function of the ASI is to identify, classify and quantify the degree of cellular atypia. This makes the ASI a valuable tool for monitoring and detecting cellular changes in either a single cell or a population of cells, and recognized.
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> [Greeberg at 171]

266. Accordingly, claims 11, 14 and 15 are anticipated by Greenberg.

6. The Claims of the '377 patent are invalid in view of Cytyc's work on the CDS-1000

267. As noted earlier in this report, Cytyc began work on an automated cytology instrument (CDS-1000) in the late 1980's. I have considered the status of the CDS-1000 as of the filing date of the '377 patent and the activity that Cytyc undertook to bring the CDS-1000 to a commercial embodiment that was shown at trade shows in late 1990, late 1991, and in October 1992. A copy of the brochure from the 1992 trade show "The ThinPrep Processor and the CDS-1000 Cytology WorkStation" is attached as Exhibit 54. ["CDS-1000 Brochure"]

268. As described in the brochure, the CDS-1000 cytology workstation consists of separate scanning and screening stations. The scanning station includes a Macintosh computer and imaging electronics. A high speed image processor uses "mathematical morphology" to analyze the images obtained by the imaging electronics. The imaging system also measures the nuclear area, nuclear shape and optical density of the nucleus and the cytoplasm. The results of the analysis are presented to a cytotechnologist by a display screen. More specifically, 48 objects are displayed that represent the cells with an elevated chance of being abnormal relative to the other cells on the slide. "All 48 objects *must* be reviewed before the case can be signed out – this interlock provides a quality control feature." [CDS-1000 brochure at 1982, italics in the original]

269. As early as December 1988, Cytyc was working on the automated cytology product that became the CDS-1000. As described in a memo dated December 30, 1988, a copy of which is attached as Exhibit 55, the product

> "displays the suspect areas of the slide on the Macintosh screen for cytotech rescreening. In this mode the concept of the false positive doesn't exist. Rather, the benefit of the system is measured in productivity improvement. A cytotech may have to review 100 cells presented on the screen rather than 20,000 on the slide for each slide. If the review of the 100 cells is much faster than the primary examination on the slide, the system is beneficial. This mode is alternately called *computer-assisted cytology*. With the addition of a large disk, off-line review may be performed.
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> [Exhibit 55, page 2]

270. The CDS-1000 was a substantial part of the operations plan for Cytyc in 1989. See, e.g., the memo entitled 1989 Operations Plan dated January 12, 1989, a copy of which is attached as Exhibit 56. I note that section 2.1 includes the timeline for activity on the imaging cytometer.

271. Finally, I have reviewed a module of the CDS-1000 code that relates to ranking the nucleus, entitled "RankNuc" a copy of which is attached as Exhibit 57. The earliest date on the code is July 25, 1989. Based on my review of the contents of code timeline, the ranking of the nucleus was a part of the original code. Additionally, the descriptive title strongly suggests that ranking nucleus was part of the Cytyc development of the CDS-1000 at least as early as July 25, 1989.

272. I note that the early documentation of the CDS-1000 is over 15 years old. I understand that much of the early documentation has not been retained because of other development projects. I have discussed the CDS-1000 development with David Zahniser and based on my conversations, and the above documents, it is my opinion Cytyc not only had the conceptual design of the CDS-1000 but also was well into the development of the CDS-1000 before October 1989. Specifically, Cytyc developers, including David Zahniser who led the CDS-1000 development team, were in the process of reducing to practice and developing a commercial computer-assisted cytology review machine that imaged cells, graded cells based on abnormality and presented the 48 "least normal cells" to a cytologist for a human review. To the extent that the invention claimed in the '377 patent is interpreted to cover the TIS system, Cytyc had developed such a system prior to the filing date of the '377 patent.

273. Cytyc worked diligently to reduce the invention to practice. As demonstrated by the following documents, Cytyc's work with the CDS-1000 processor continued at least through the time when the CDS-1000 was displayed in 1990, 1991 and 1992. I understand that due to the passage of time that some of the documents for the CDS-1000 are no longer available. I have

reviewed the documents that Cytyc has been able to identify.[20] Many of the documents represent days and months of work by teams of people.

274. I have discussed the development of the CDS-1000 with Dr. David Zahniser. Based on the documents I have reviewed and my conversations with Dr. Zahniser, I believe that Cytyc did not abandon, suppress or conceal the development of the CDS-1000. On the contrary, the CDS-1000 was presented at multiple trade shows and was warmly received by the cytology industry at the time and presented at multiple trade shows. I understand that the CDS-1000 system, and computer assisted screening in general, continued at a reduced level in 1993 while the company focused on a thin layer slide preparation technique.

7. The Asserted Claims are Obvious In View Of CDS-1000 and the Prior Art Described in This Report

275. To the extent that TriPath argues that the CDS-1000 fails to disclose each feature of the patent claims, the missing elements are disclosed in the prior art described in this report. Further, the Cytyc team leader, Dr. Zahniser, has published extensively, including his doctoral thesis, in the filed. His dissertation, "Development of a Fully Automatic System for Prescreening Cervical Smears BioPEPR", was completed 1979 and is produced at Bates No. C0096799-928. Dr. Zahniser's extensive work in the field in the 1970's and 1980's combined with the CDS-1000 documents renders the invention claimed in the '377 patent invalid. The combination is suggested by the prior art that describes the interactive review and ranking, which is described more fully above.

[20] I have reviewed the following documents that are relevant to the development and publication of the CDS-1000 device: C0065268-90, C0074813-15, C0075231-33, C0075236-38, C0075250-56, C0076406-39, C0076629-40, C0076911-12, C0081467-517, C0081554-88, C0082345-50, C0082366-68, C0082369-77, C0082422-26, C0083049-124, C0083299-305, C0083306-9, C0083312-15, C0083320-21, C0083327-29, C0083354-7, C0083370-73, C0083406-8, C0083420-30, C008347576, C0083580-90, C0083680-93, C0083772-84; C0083800-10,

8. Secondary Considerations of Obviousness

276. The CDS-1000 paragraphs above are also relevant to the patentability of the claims of the '377 patent as a secondary consideration of obviousness. Specifically, Cytyc can demonstrate that the CDS-1000 was well into the development process when the '377 patent was filed. Indeed, the ranking feature that was discussed at length in the prosecution history of the '377 patent was already in a computer program module 3 months before the date which TriPath asserts is the earliest date of the invention, October 11, 1989.

9. Invalidity based on Obviousness

277. If TriPath attempts to argue that the references described above do not anticipate the claims, the references cited above, alone or in combination, render the claims invalid due to obviousness. For example, if TriPath seeks construction of a claim term such that the claim limitation is disclosed in some but not all of the references above, I reserve the right to argue that the claims are obvious in view the group of references above.

IX. Trial Exhibits

278. I may rely on visual aids and demonstrative exhibits that demonstrate the bases of my opinions. Examples of these visual aids and demonstrative exhibits may include, for example, claim charts, patent drawings, excerpts from patent specifications, file histories, interrogatory responses, deposition testimony and deposition exhibits, as well as charts, diagrams, videos and animated or computer-generated video.

C0083861-64, C0083896, C0089612-17, C0093989-4071, C0094321-24, C0103018-63, C0103064-3215, C0139750-67, C0139768-85, C0139786-95, C0139796-809, C0139810-21, C0139822-28, C0139829-40, C0139841-50, C0139851-56, C0139857-91, C0139989-93, C0141289-467.